INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/26309

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/70; C12Q 1/68; C12N 15/63
US CL : 435/6, 320.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6, 320.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category.*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,448,007 B1 (GIORDANO et al.) 10 September 2002 (10.09.2002), see entire document.	1-24, 41, 43-49
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A		31-35, 37-40, 42, 50-54
Y	US 5,859,227 A (GIORDANO et al.) 12 January 1999 (12.01.1999), see entire document.	1-24
Y	ISMAEL et al. Split-intron retroviral vectors: enhanced expression with improved safety. J Virol., March 2000, Vol. 74, No. 5, pages 2365-2371.	1-24
A	US 6,465,176 B1 (GIORDANO et al.) 15 October 2002 (15.10.2002), see entire document.	31-35, 37-54
A	US 5,928,888 A (WHITNEY) 27 July 1999 (27.07.1999), see entire document.	31-35, 37-54

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 June 2005 (18.06.2005)	13 JUL 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Daniel M. Sullivan J. Roberts for Telephone No. (571) 272-1600

Form PCT/ISA/210 (second sheet) (January 2004)

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-24 (in part), 31-35 and 37-54

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☒ No protest accompanied the payment of additional search fees.

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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-24, drawn to A nucleic acid construct comprising a high-level mammalian expression vector and a nucleic acid sequence encoding a reporter polypeptide wherein said nucleic acid sequence encoding a reporter polypeptide is linked to an iron response element.

Group II, claim(s) 1-24, drawn to A nucleic acid construct comprising a high-level mammalian expression vector and a nucleic acid sequence encoding a reporter polypeptide wherein said nucleic acid sequence encoding a reporter polypeptide is linked to an internal ribosomal entry site.

Group III, claim(s) 1-24, drawn to A nucleic acid construct comprising a high-level mammalian expression vector and a nucleic acid sequence encoding a reporter polypeptide wherein said nucleic acid sequence encoding a reporter polypeptide is linked to an upstream open reading frame.

Group IV, claim(s) 1-24, drawn to A nucleic acid construct comprising a high-level mammalian expression vector and a nucleic acid sequence encoding a reporter polypeptide wherein said nucleic acid sequence encoding a reporter polypeptide is linked to a male specific lethal element.

Group V, claim(s) 1-24, drawn to A nucleic acid construct comprising a high-level mammalian expression vector and a nucleic acid sequence encoding a reporter polypeptide wherein said nucleic acid sequence encoding a reporter polypeptide is linked to a G-quartet element.

Group VI, claim(s) 1-24, drawn to A nucleic acid construct comprising a high-level mammalian expression vector and a nucleic acid sequence encoding a reporter polypeptide wherein said nucleic acid sequence encoding a reporter polypeptide is linked to a 5'-terminal oligopyrimidine tract.

Group VII, claim(s) 25-30, drawn to A method of making a nucleic acid construct comprising cloning a gene and a vector in said nucleic acid construct, engineering said nucleic acid construct to prevent an expressed gene product form having a UTR not found in a target gene and linking a target UTR to said gene.

Group VIII, claim(s) 31-34, 41-54, drawn to A method of screening for a compound that modulates expression of a polypeptide comprising maintaining a cell comprising a nucleic acid molecule comprising a gene encoding a reporter polypeptide flanked by a target 5' UTR and a target 3' UTR, forming a complex with the UTR and detecting the effect of a compound on the UTR-complex.

Group IX, claim(s) 35 and 37-40, drawn to A method of screening in vivo for a compound that modulates UTR-dependent expression comprising providing a cell having a high-expression constitutive promoter upstream of a target 5' UTR, said target 5' UTR upstream from a nucleic acid encoding a reporter polypeptide, said nucleic acid encoding a reporter polypeptide upstream of a 3' UTR, contacting the cell with a compound, and detecting the reporter polypeptide.

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Group X, claim(s) 36, drawn to A method of screening in vitro for a compound that modulates UTR-affected expression comprising providing an in vitro translation system, contacting the in vitro translation system with a compound and a nucleic acid sequence comprising a target 5' UTR, said target 5' UTR upstream from a nucleic acid encoding a reporter polypeptide, said nucleic acid encoding a reporter polypeptide upstream of a 3' UTR, and detecting said reporter polypeptide in vitro.

The inventions listed as Groups I-X do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The inventions listed as Groups I-X do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. The Groups are united by the technical feature of a nucleic acid construct comprising a high-level mammalian expression vector and a nucleic acid sequence encoding a reporter polypeptide linked to one or more target UTRs, which target UTRs include an internal ribosomal entry site. On page 7 of the specification, reporter gene is defined as any gene whose expression can be measured. Thus, the unifying technical feature reads on any high-level mammalian expression vector comprising a nucleic acid sequence encoding a gene whose expression can be measured (essentially all genes, since the expression of any gene can be measured by northern blotting) linked to an IRES. WO 98/37189 teaches a high-level mammalian expression vector comprising a nucleic acid sequence encoding a gene whose expression can be measured operably linked to an IRES. Thus, the technical feature that unites the Groups is not a contribution over the art and the claims lack a unifying special technical feature.

The special technical feature of Group I is considered to be a reporter polypeptide linked to an iron response element, which technical feature is not shared by the nucleic acid construct of the other Groups.

The special technical feature of Group II is considered to be a reporter polypeptide linked to an internal ribosomal entry site, which technical feature is not shared by the nucleic acid construct of the other Groups.

The special technical feature of Group III is considered to be a reporter polypeptide linked to an upstream open reading frame, which technical feature is not shared by the nucleic acid construct of the other Groups.

The special technical feature of Group IV is considered to be a reporter polypeptide linked to a male specific lethal element, which technical feature is not shared by the nucleic acid construct of the other Groups.

The special technical feature of Group V is considered to be a reporter polypeptide linked to a G-quartet element, which technical feature is not shared by the nucleic acid construct of the other Groups.

The special technical feature of Group VI is considered to be a reporter polypeptide linked to a 5'-terminal oligopyrimidine tract, which technical feature is not shared by the nucleic acid construct of the other Groups.

The special technical feature of Group VII is considered to be engineering said nucleic acid construct to prevent an expressed gene product from having a UTR not found in a target gene and linking a target UTR to said gene, which process steps are not comprised by the methods of Groups VIII-X.

The special technical feature of Group VIII is considered to be forming a complex with the UTR and detecting the effect of a compound on the UTR-complex, which process steps are not comprised by the methods of Groups VII, IX and X.

The special technical feature of Group IX is considered to be providing a cell having a high-expression constitutive promoter upstream of a target 5' UTR, said target 5' UTR upstream from a nucleic acid encoding a reporter polypeptide, said nucleic acid encoding a reporter polypeptide upstream of a 3' UTR, contacting the cell with a compound, and detecting the reporter polypeptide, which process steps are not comprised by the methods of Groups VII, VIII and X.

The special technical feature of Group X is considered to be providing an in vitro translation system, contacting the in vitro translation system with a compound and a nucleic acid sequence comprising a target 5' UTR, said target 5' UTR upstream from a nucleic acid encoding a reporter polypeptide, said nucleic acid encoding a reporter polypeptide upstream of a 3' UTR, and detecting said reporter polypeptide in vitro, which process steps are not comprised by the methods of Groups VII-IX.

Accordingly, Groups I-X are not so linked by the same or corresponding special technical feature as to for a single general inventive concept.

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Continuation of B. FIELDS SEARCHED Item 3:
APS (EAST); STN (MEDLINE BIOSIS CAPLUS EMBASE CANCERLIT)
KEYWORDS: UTR, iron response element, intron screen